We Claim

1. An isolated lysolipid (LL) receptor/EDG receptor which is expressed endogenously in HeLa cells and upon activation results in increased induction of IL-8 or NF-kB with the proviso that the isolated EDG receptor is not an EDG-2 or rat EDG-4 receptor.

2. The isolated LL/EDG receptor of claim 1 which is expressed endogenously in HeLa cells and that upon activation by edelfosine results in increased IL-8 or NF-κB induction.

3. An isolated EDG receptor that upon activation results in increased induction of IL-8 or NF-kB with the proviso that the isolated EDG receptor is not an EDG-2 or rat EDG-4 receptor.

4. The isolated EDG receptor of claim 3 wherein said receptor is activated by a lysolipid selected from one or more of the group consisting of LPA, S1P and SPC.

5. The isolated EDG receptor of claim 4 wherein the said receptor is the human EDG-4 receptor and it is activated by S1P and SPC.

6. An isolated nucleotide sequence encoding the receptor as defined in claim 3.

7. A method of identifying a compound as an agonist for a receptor as defined in claim 3, comprising the steps of:

(a) culturing cells which express the receptor of claim 1-5 or 8 in medium with low-serum or defined medium designed to reduce basal levels of NF-κB activation;

(b) contacting said cultured cells with said compound to be tested for agonist activity at said receptor; and

(c) measuring a response indicative of the degree of NF-κB activation.

8. A method according to claim 7 wherein said receptor is selected from one or more of the group consisting of EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6.

9. The agonist as identified by the method of claim 8.

10. A pharmaceutical composition containing the agonist of claim 9 and a pharmaceutically acceptable excipient.

11. A method of treating an inflammatory process condition in a subject comprising administering an effective amount of the pharmaceutical composition of claim 10 for upregulation of the inflammatory process, respectively.

12. A method of modulating an immune response in a subject comprising administering an effect amount of the pharmaceutical composition of claim 10 for upregulation of the immune response.

13. A method of identifying a compound as an agonist for a receptor as defined in claim 3, comprising the steps of:

(a) culturing cells which express the receptor of claim 3 in a medium with low-serum or defined medium designed to reduce basal levels of IL-8 production;

(b) contacting said cultured cells with a candidate compound to be tested for agonist activity at said receptor; and

(c) measuring a response indicative of the degree of IL-8 production.

14. A method according to claim 13 wherein said receptor is selected from one or more of the group consisting of EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6.

15. The agonist as identified by the method of claim 14.

16. A pharmaceutical composition containing the agonist of claim 15 and a pharmaceutically acceptable excipient.

17. A method of identifying a compound as an antagonist for a receptor as defined in claim 3, comprising the steps of:

(a) culturing cells which express the receptor of claim 3 in medium with low-serum or defined medium designed to reduce basal levels of NF-κB activation;

(b) contacting said cells with a mixture comprising an agonist and said compound to be tested for antagonist activity at said receptor, wherein said agonist is selected from a LL or 20% FBS; and

(c) measuring a response indicative of the degree of NF-κB activation.

18. The method of claim 17 wherein said receptor is selected from the group comprising EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6.

19. The antagonist as identified by the method of claim 18.

20. A pharmaceutical composition containing the antagonist as defined in claim 19 and a pharmaceutically acceptable excipient.

21. A method of treating an inflammatory process condition in a subject comprising administering an effective amount of the pharmaceutical composition of claim 20 for downregulation of the inflammatory process.

22. A method of modulating an immune response in a subject comprising administering an effect amount of the pharmaceutical composition of claim 20 for downregulation of the immune response.

23. A method of identifying a compound as an antagonist for a receptor as defined in claim 3 comprising the steps of:
(a) culturing cells which express the receptor of claim 3 in medium with low-serum or defined medium designed to reduce basal levels of IL-8 production;
(b) contacting said cells with a mixture comprising an agonist and said compound to be tested for antagonist activity at said receptor, wherein said agonist is an LL or 20% FBS; and
(c) measuring a response indicative of the degree of IL-8 production .

24. The method of claim 21 wherein said receptor is selected from the group comprising EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6.

25. The antagonist as identified by the method of claim 22.

26. A pharmaceutical composition containing the antagonist as defined in claim 23 and a pharmaceutically acceptable excipient.

27. A method of controlling apoptosis in a cell comprising a receptor as defined in claim 3 comprising the step of contacting said cell with an effective amount of an agonist of claim 9.

28. A method of controlling apoptosis in a cell comprising a receptor as defined in claim 3 comprising the step of contacting said cell with an effective amount of an antagonist of claim 19.

29. A method of determining whether an expressible DNA sequence encodes an EDG receptor that upon activation by a suitable EDG receptor ligand results in increased NF-κB or IL-8 activation, comprising:

(a) identifying a cell that does not exhibit increased NF-κB activation when contacted with said ligand;

(b) transfecting said cell with said expressible DNA sequence; and

(c) contacting said transfected cell with said ligand and measuring the resulting NF-κB or IL-8 activation.

30. A method according to claim 29 wherein said ligand is selected from one or more of the group comprising LPA, S1P, SPC, psychosine, glucopsychosine, dihydro-S1P and edelfosine.

31. An isolated nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence comprising nucleotides 38- 1099 of Figure 15A;

(b) the nucleotide sequence of Figure 15B;

(c) a nucleotide sequence with at least about 95% sequence identity to (a) or (b) and which hybridizes under stringent conditions to sequences (a) and (b), respectively;

(d) a nucleotide sequence which encodes the amino acid sequence for the human EDG-4 receptor of Figure 16A; and

(e) a nucleotide sequence which encodes the amino acid sequence for the human EDG-4 receptor of Figure 16B.

32. A human EDG-4 receptor encoded by the nucleotide sequence of claim 3.

33. An expression vector comprising the nucleotide sequence of claim 3.

34. A host cell transformed with the expression vector of claim 5.